

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
18 September 2003 (18.09.2003)

PCT

(10) International Publication Number
WO 03/076424 A1

(51) International Patent Classification?: C07D 313/00, A61K 31/335, A61P 29/00, C07D 225/06, 407/12, 491/04, 267/00, 493/04, A61K 31/36, 31/395, A61P 11/06, 17/06, 17/16, 19/04, 35/00, 37/06

(21) International Application Number: PCT/US03/07377

(22) International Filing Date: 7 March 2003 (07.03.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/362,883 8 March 2002 (08.03.2002) US
60/380,711 14 May 2002 (14.05.2002) US

(71) Applicant (for all designated States except US): EISAI CO. LTD. [JP/JP]; 6-10, Koishikasa 4-Chome, Bunkyo-ku., Tokyo, 112-8088 (JP).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BOIVIN, Roch [CA/US]; 11 Oakland Road, Lawrence, MA 01843 (US). CHIBA, Kenichi [JP/JP]; 5-20-401, Oomachi, Tsuchiura-shi, Ibaraki (JP). DAVIS, Heather, A. [CA/US]; 202 Morgan Drive, Haverhill, MA 01832 (US). DIEPITRO, Lucian [US]; 62 Mill Street, Apt 4, Woburn, MA 01801 (US). DU, Hong [CN/US]; 43 Upland Street, North Andover, MA 01845 (US). EGUCHI, Yoshihito [JP/JP]; 233-38, Toyoshiki, Kashiwa-shi, Chiba (JP). FUJITA, Masanori [JP/JP]; 128-3-6, Hitachinonishi, Ushiku-shi, Ibaraki (JP). GILBERT, Sandra [US]; 35 Merlino Drive, Groton, CT 06340 (US). GOTO, Masaki [JP/JP]; 1141-21, Naka, Tsuchiura-shi, Ibaraki (JP). HARMANGE, Jean, Christophe [FR/US];

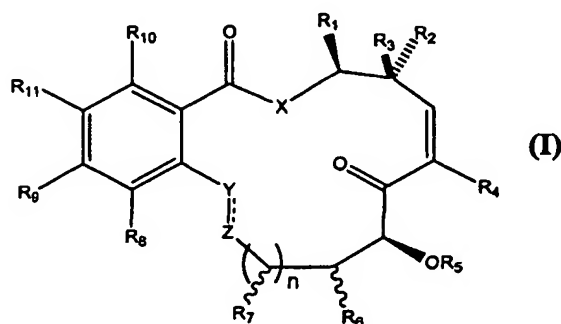
57 William Street, Andover, MA 01810 (US). INOUE, Atsushi [JP/JP]; 2-10-15 Matsuhira, Tsukuba-shi (JP). JIANG, Yimin [US/US]; 16 Devonshire Lane, Londonderry, NH (US). KAWADA, Megumi [JP/JP]; 4-9 Kamiya 2-chome, Ushiku-shi, Ibaraki (JP). KAWAI, Takatoshi [JP/JP]; 2-11-33, Higashi, Tsukuba-shi, Ibaraki (JP). KAWAKAMI, Yoshiyuki [JP/JP]; 3-6-2 Tokodai, Tsukuba-shi, Ibaraki (JP). KIMURA, Akifumi [JP/JP]; 7-2, Inarimae, Tsukuba-shi, Ibaraki, Ibaraki (JP). KOTAKE, Makoto [JP/JP]; 144-3-515, Abiko, Abiko-shi, Chiba (JP). KUBOI, Yoshikazu [JP/JP]; 2-13-14, Matsushiro, Tsukuba-shi, Ibaraki (JP). LEMELIN, Charles [US]; Andover, MA (US). LI, Xiang-Yi [US/US]; 229 High Plain Road, Andover, MA 01810 (US). MATSUSHIMA, Tomohiro [JP/JP]; 10-2, Tagu 2-chome, Ushiku-shi, Ibaraki (JP). MIZUI, Yoshiharu [JP/JP]; 10-2, Tagu 2 chome, Ushiku-shi, Ibaraki (JP). SAKURAI, Hideki [JP/JP]; 4-8-3 Ninomiya, Tsukuba-shi, Ibaraki (JP). SCHILLER, Shawn [US/US]; 614 Hilldale Avenue, Haverhill, MA 01832 (US). SHEN, Yongchun [CN/US]; 21 Villa Roma Drive, Tewksbury, MA 01876 (US). SPYVEE, Mark [GB/US]; 75 Laura Lane, Hampstead, NH 03841 (US). TANAKA, Isao [JP/JP]; 2-5-16, Ninomiya, Tsukuba-shi, Ibaraki (JP). WANG, Yuan [US/US]; 344 River Road, Andover, MA 01810 (US). YAMAMOTO, Satoshi [JP/JP]; 3-9-7, Misono, Moriya-shi, Ibaraki (JP). YONEDA, Naoki [JP/JP]; 1-906-306, Takezono, Tsukuba-shi, Ibaraki 305-0032 (JP). KOBAYASHI, Seiichi [JP/US]; 28 Trowbridge Street, Belmont, MA 02478 (US).

(74) Agent: LAGNEAU, Nadege, M.; Choate, Hall & Stewart, Exchange Place, 53 State Street, Boston, MA 02109 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

[Continued on next page]

(54) Title: MACROCYCLIC COMPOUNDS USEFUL AS PHARMACEUTICALS



(57) Abstract: The present invention provides compounds having formula (I), and additionally provides methods for the synthesis thereof and methods for the use thereof in the treatment of various disorders including inflammatory or autoimmune disorders, and disorders involving malignancy or increased angiogenesis, wherein R₁ -R₁₁, t, X, Y, Z, and n are as defined herein.

WO 03/076424 A1



GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

- (84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.